ELSEVIER

Pharmacology, Biochemistry and Behavior 72 (2002) 681–689

PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR

www.elsevier.com/locate/pharmbiochembeh

Mood differences between male and female light smokers and nonsmokers

Sandra E. File*, Abigail K. Dinnis, Joy E. Heard, Elaine E. Irvine

Psychopharmacology Research Unit, Centre for Neuroscience, Hodgkin Building, GKT School of Biomedical Sciences, King's College London, Guy's Campus, London SE1 1UL, UK

Received 27 November 2001; received in revised form 17 January 2002; accepted 21 January 2002

Abstract

In an open study, we determined whether there were sex differences in the mood ratings of non-deprived light smokers and nonsmokers under baseline conditions and after completing a battery of cognitive tests that were mildly stressful. Male and female students who were light smokers (5–12 cigarettes a day) were tested immediately after smoking their usual cigarette, at a time that they normally smoked. They were compared with a group of male and female students who were nonsmokers and did not differ on age, IQ, personality measures, anxiety or depression. Compared with the nonsmokers, both male and female smokers felt overall significantly more discontented, troubled, tense, quarrelsome, furious, impatient, hostile, annoyed and disgusted and experienced greater dizziness. The performance of distracting cognitive tasks did not reveal anxiolytic effects of smoking, and after performance of these tasks, both smokers and nonsmokers became more discontented and anxious. In addition, after the cognitive testing, both male and female smokers showed greater increases than nonsmokers in feeling spiteful, rebellious, incompetent and in sweating, suggesting that they experienced greater mood changes in response to cognitive stress. There were no overall differences between the smokers and nonsmokers in the performance of divided or sustained attention tasks or in episodic memory. It is unlikely that either nicotine withdrawal or differences in cognitive performance could account for the greater anxiety, discontent and aggressive mood that was found in smokers. © 2002 Elsevier Science Inc. All rights reserved.

Keywords: Smoking; Sex differences; Stress; Mood; Aggression; Anxiety; Memory; Attention

1. Introduction

About 28% of the British population still smoke, and in recent years, teenage girls have accounted for the majority of new smokers (Royal College of Physicians, 2000). Adolescent smokers report significantly higher levels of nervousness, stress and anxiety than do age-matched nonsmokers and 64% of adolescent female smokers report feeling calmer after smoking (Royal College of Physicians, 2000). Smokers have been found to have higher levels of neuroticism and neurotic traits (anxiety, depression and anger) than nonsmokers (Spielberger and Jacobs, 1982; Gilbert and Gilbert, 1995). Anda et al. (2000) have shown that young adult smokers are significantly more depressed than nonsmokers, even when matched for adverse life events and teenage smokers are more depressed than nonsmokers. However, it is difficult to determine causality from these observations. It could be that preexisting mood differences contribute to the initiation of smoking, and, at least, in some cases, that smoking is initiated as a means of self-medicating negative mood states (Gilbert and Gilbert, 1995; Sonntag et al., 2000). Results from animal studies suggest that nicotine might have biphasic effects on anxiety, with low doses reducing, and high doses enhancing, anxiety (File et al., 1998). It is thus also possible that the effects of nicotine itself might contribute to negative mood states (see Parrott, 1999). Perkins et al. (1994) found that, compared with placebo, nicotine increased subjective tension, even in smokers. Breslau et al. (1998) have shown that depression increases in youngsters who take up smoking, and when smokers give up smoking, they report better mood and lower anxiety after the first week of abstinence (Hughes et al., 1990; West and Hajek, 1997). Thirdly, it could be that the increased incidence of negative mood (anxiety, depression and anger) in smokers can be explained by mood changes during repeated periods of nicotine withdrawal (Hughes et al., 1984, 1991, Parrott, 1994, 1995; Heishman et al., 1994; Warburton and Mancuso, 1998). Finally, there is evidence that common genetic

* Corresponding author. Tel.: +44-20-7848-6667; fax: +44-20-7848-6660.

E-mail address: sandra.file@kcl.ac.uk (S.E. File).

0091-3057/02/$ – see front matter © 2002 Elsevier Science Inc. All rights reserved.
PII: S0091-3057(02)00733-5

PM3003745711

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

factors might influence vulnerability to both smoking and depression (Quattrocki et al., 2000).

There are relatively few studies that have focussed on possible sex differences in response to nicotine, but, in general, females seem less sensitive than males to the reinforcing effects of nicotine (see Perkins et al., 1999 for review). Positive correlations have been found between testosterone levels in females and cigarette use in adolescence and young adulthood (Martin et al., 2001), raising the possibility that testosterone might be an important direct or indirect mediator of nicotine's reinforcing effects. In contrast, animal experiments suggest that female adolescent rats are more sensitive than males to the anxiolytic effects of nicotine (Cheeta et al., 2001). This possibility was supported by recent findings of sex differences in mood changes induced by nicotine after stress. File et al. (2000, 2001) found that, in nonsmokers, nicotine had calming effects after stress in young female students, whereas in male students, it enhanced ratings of anxiety, aggression and discontent.

The purpose of the present study was not to examine the effects of nicotine in smokers (e.g. by comparing mood before and after abstinence), but to explore possible sex differences in mood between nondeprived light smokers and nonsmokers before and after completing a battery of cognitive tests. Kassel and Unrod (2000) found that smoking reduced anxiety when smokers were engaged in a distracting task, and they interpreted this as evidence that nicotine's anxiolytic effects were secondary to improved attention. In other words, smoking reduces anxiety by concentrating attention on immediately salient stimuli associated with the task and away from distressing thoughts. It was therefore possible that smokers would experience a different pattern of mood changes after completion of the cognitive tests than would nonsmokers and that there might be sex differences in these changes. In previous studies (e.g. File et al., 2001) it has been found that performance of this cognitive test battery was stressful, insofar as it increased ratings of anxiety, discontent and aggression. The mood ratings were completed before the cognitive tests (prestress) and at the end of testing (poststress), thus allowing determination of the effects of cognitive stress on mood. It was after the stress of cognitive testing that sex differences emerged in response to nicotine in nonsmokers, with females showing an anxiolytic response to nicotine, but males showing increased anxiety and aggression (File et al., 2001).

2. Materials and methods

2.1. Subjects

Thirty-six medical students (9 female smokers and 9 female nonsmokers, 8 male smokers and 10 male nonsmokers) were recruited to the study and were told that the study would compare the performance of smokers and nonsmokers on cognitive tests. No mention was made of the purpose to assess mood changes. The students were paid £10 for their participation. The study was approved by the Guy's Hospital Research Ethics Committee and all volunteers gave written informed consent. All the volunteers were healthy and medication free at the time of testing and had not consumed any caffeine-containing beverages for 2 h before testing. The smokers smoked between 5 and 12 cigarettes a day and had done so for at least a year. None of the nonsmokers smoked cannabis, and smokers who also smoked cannabis were excluded from the study. This resulted in the exclusion of several students, but as a result, none of the subjects that we tested were users of Ecstasy or any other illicit drug.

2.2. Procedure

2.2.1. Rating scales

An estimate of verbal IQ was obtained using the National Adult Reading Test revised version (NART-R; Nelson and Willison, 1991). Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HAD; Zigmond and Snaith, 1983), and extraversion and neuroticism were measured using the Eysenck Personality Questionnaire (Eysenck and Eysenck, 1976). Testing was scheduled for each smoker at a time they would normally smoke and this was most typically after 1–2 h of abstinence. Testing began 5 min after smoking all of their usual cigarette (for the smokers only). First, the volunteers completed analogue mood and aggression rating scales (Bond and Lader, 1974, 1986), by placing a vertical line across each 100-mm horizontal line between two opposite adjectives. They then completed analogue ratings of bodily symptoms. The ratings completed at this stage are the 'prestress' ratings. All the rating scales were again completed at the conclusion of the cognitive testing and constituted the 'poststress' ratings.

2.2.2. Cognitive tests

Volunteers were shown 20 pictures, each for 3 s, and told to name each one and to try and remember as many as possible as they would be asked to recall them about 20 min later. They were then given the digit–symbol substitution (DSS) test, which is a subtest of the WAIS-R (Weschler, 1981) and is a measure of attention and psychomotor speed. Volunteers were given a sheet of paper with the digits 1–9 in random order. With the use of a key containing a corresponding symbol for each digit, the task was to place the correct symbol in the empty box below each digit. This task lasted for 3 min, and at the same time, volunteers had to perform a second task, that of counting the number of gaps that there were in the music that was played during the DSS task. This therefore provided a test of divided attention. In the delayed matching to sample (DMTS; Owen et al., 1995) test from the Cambridge Neuropsychological Test Automated Battery (CANTAB; CeNeS, Cambridge), initially, a pattern was shown on a computer screen, simultaneously with a choice of four patterns. The latency to select the

PM3003745712

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

Table 1
Mean (±S.E.M.) age, estimated IQ (NART_R), extraversion and neuroticism (Eysenck Personality Questionnaire), anxiety and depression (Hospital Anxiety and Depression scale), daily cigarette consumption and daily caffeine (expressed as cups of instant coffee) and weekly alcohol (U) intake of female and male smokers and nonsmokers

	Smoker		Nonsmoker	
	Female	Male	Female	Male
Age	20.4±0.4	21.1±0.3	20.4±0.2	21.2±0.5
IQ	108.9±2.3	110.4±1.8	111.1±2.3	111.9±2.5
Extraversion	15.2±0.8	16.3±1.6	14.0±1.4	14.8±1.7
Neuroticism	8.4±1.0	8.8±2.2	10.8±1.5	7.4±1.3
Anxiety	7.1±0.4	6.8±2.1	6.7±1.2	4.4±0.7
Depression	2.3±0.8	1.8±0.8	1.8±0.3	1.1±0.4
Caffeine (cups/day)	3.0±0.8	5.3±0.9	2.3±1.7	3.0±2.8
Alcohol (U/week)	17.0±3.5	23.9±6.1	9.0±4.7	20.1±5.0
Cigarettes/day	8.1±1.0	8.5±1.1	0	0

correct pattern was recorded. A series of test patterns were then shown, but each then disappeared for 4 or 12 s before being replaced with a choice of four patterns. The latencies to respond correctly were recorded. In the rapid visual information processing test (RVIP; Wesnes and Warburton, 1983) a series of digits was presented on a computer screen at a rate of 100 digits/min. The task was to respond as quickly as possible when three consecutive odd or even numbers were shown. Each block lasted for 1 min, and there were four blocks of nine series of digits, thus, the maximum number of correct responses (hits) was 36. The Paced Auditory Serial Addition Test (PASAT) measures sustained attention (Spreen and Strauss, 1991). This involves adding together successive pairs of digits read from a list of 61 numbers, presented at different speeds from one digit every 2.4 s (Tape A) to one digit every 1.2 s (Tape D). The total number of correct responses (maximum 60) was recorded for each trial. Long-term episodic memory was measured by presenting a set of 20 pictures of common objects, each picture was shown for 3 s, and then 20 min later, the volunteers were asked to recall as many of these as possible.

2.3. Statistics

The data were analysed by two-way analyses of variance with smoking status and sex as the two independent factors. Where there were repeated measures (as in the mood ratings or the PASAT), three-way between–within analyses of variance were conducted. A significant difference between smokers and nonsmokers would be revealed by a significant main effect of smoking status. If the effect of smoking differed for males and females there would be a significant Sex × Smoking Status interaction. A significant influence of the cognitive stress would be revealed by a significant stress factor, and an interaction between stress and smoking status would show a difference in response to stress between smokers and nonsmokers. A significant interaction between stress and sex would show a sex difference in response to stress that was independent of smoking status. Probability levels are cited for results close to or reaching significance, otherwise, nonsignificant effects are indicated by ns. Error scores on the cognitive tests were analysed by nonparametric Mann–Whitney U tests since the number of zero scores skewed the distribution.

3. Results

3.1. Group characteristics

The groups did not differ significantly on age, IQ, extraversion or introversion [$F(1,32)<1.0$, ns in all cases], or in anxiety or depression [$F(1,32)<1.4$, ns in both cases] (see Table 1). They did not differ significantly in their daily consumption of caffeine-containing drinks, but there were trends for the smokers to consume more caffeine [$F(1,32)=3.4$, $P<.10$] and for males to consume more than females [$F(1,32)=3.4$, $P<.10$]. Because almost all the caffeine consumption was instant coffee, the caffeine intake has been standardised as cups of coffee. There was no significant difference between smokers and nonsmokers in their weekly alcohol consumption [$F(1,32)=1.9$, ns], but males drank more than females [$F(1,32)=4.4$, $P<.05$].

3.2. Mood ratings

3.2.1. Effects of smoking status

Only one bodily symptom showed a significant difference between smokers and nonsmokers. The smokers felt significantly more dizzy than the nonsmokers [$F(1,32)=6.8$, $P=.01$]. However, there was also a trend for the smokers to have greater symptoms of sweating [$F(1,32)=3.0$, $P=.09$] and of dry mouth [$F(1,32)=3.4$, $P<.07$] (see Table 2). In all cases, these differences were found in both males and females.

From the mood scale developed by Bond and Lader (1974), three independent factors can be extracted, measuring alertness, contentment and calmness. There was no

Table 2
Mean ± S.E.M. scores on analogue rating scales of bodily symptoms and the mood factors isolated from the Bond and Lader mood scale

	Nonsmokers	Smokers
Dizzy	5.6±2.0	19.4±4.9**
Sweating	17.8±3.8	27.7±4.0***
Dry Mouth	15.0±3.8	27.9±6.1
Palpitations	18.5±3.9	20.1±3.4
Physical Tiredness	32.7±4.3	38.9±6.1
Mood Factor 1 Alertness	44.2±2.1	40.8±2.3
Mood Factor 2 Discontented	45.2±1.5	50.5±1.9*
Mood Factor 3 Anxiety	54.7±2.4	61.6±2.3***

* $P<.05$, compared with nonsmokers.
** $P<.01$, compared with nonsmokers.
*** $P<.10$, compared with nonsmokers.

PM3003745713

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

difference between the smokers and nonsmokers on the alertness factor [$F(1,32)=1.1$, ns], but the smokers were significantly less contented than nonsmokers [$F(1,32)=5.2$, $P<.03$] and less calm [$F(1,32)=3.8$, $P<.06$] (see Table 2). These differences with smoking status were reflected in several individual measures of mood and the differences were found in both males and females. Thus, the smokers were more discontented [$F(1,32)=4.3$, $P<.05$], troubled [$F(1,32)=8.5$, $P<.01$], tense [$F(1,32)=6.7$, $P=.01$] and mentally slow [$F(1,32)=4.4$, $P<.05$] (see Fig. 1). The only mood rating to show a sex difference according to smoking status was proficient [Smoking Status × Sex interaction, $F(1,32)=4.2$, $P<.05$]; this was because whereas the smoking females rated themselves as less proficient than did the nonsmoking females, in the males, the pattern was reversed.

The smokers had higher ratings on several items relating to aggressive mood and again these changes showed no sex differences. Thus, they were more quarrelsome [$F(1,32)=7.0$, $P=.01$], furious [$F(1,32)=5.0$, $P<.04$], impatient [$F(1,32)=6.4$, $P<.02$], unfriendly [$F(1,32)=6.4$, $P<.02$], annoyed [$F(1,32)=5.0$, $P<.04$ and disgusted [$F(1,32)=4.1$, $P=.05$] (see Fig. 2).

3.2.2. *Effects of cognitive stress and smoking status*

The performance of the cognitive test battery was stressful, insofar as it resulted in significantly increased ratings of feeling discontented [Stress, $F(1,32)=28.5$, $P<.001$] and anxious [Stress, $F(1,32)=71.4$, $P<.0001$], and these changes were found equally in smokers and nonsmokers and in males and females (Table 3). In addition, after the stress of cognitive testing, a few more mood differences emerged between the smokers and nonsmokers, with the smokers showing a greater response to stress (Fig. 3), but none of these differed for males and females. Thus, whilst everyone felt less proficient after the cognitive tests [Stress, $F(1,32)=22.4$, $P<.0001$], this was more marked in the smokers [Stress ×

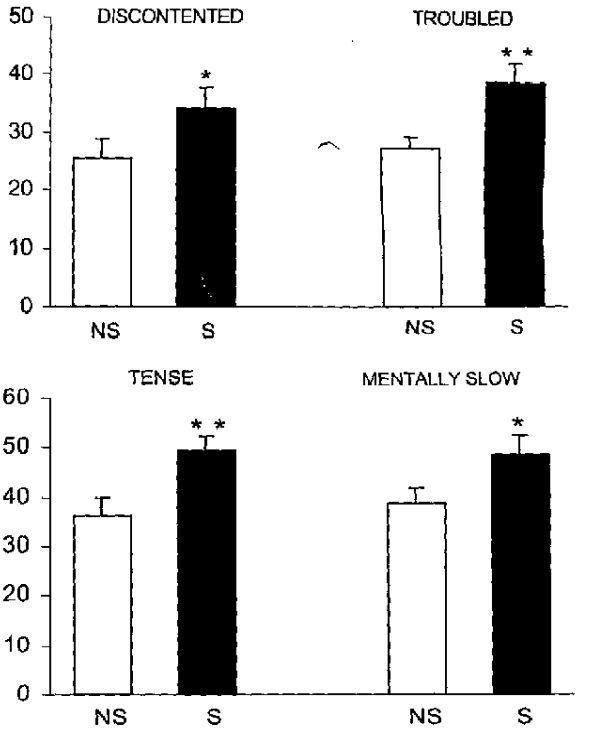

Fig. 1. Mean±S.E.M. analogue ratings (0–100 mm) of feeling discontented, troubled, tense and mentally slow of nonsmokers (NS) and smokers (S). ** $P<.01$, * $P<.05$ compared with nonsmokers.

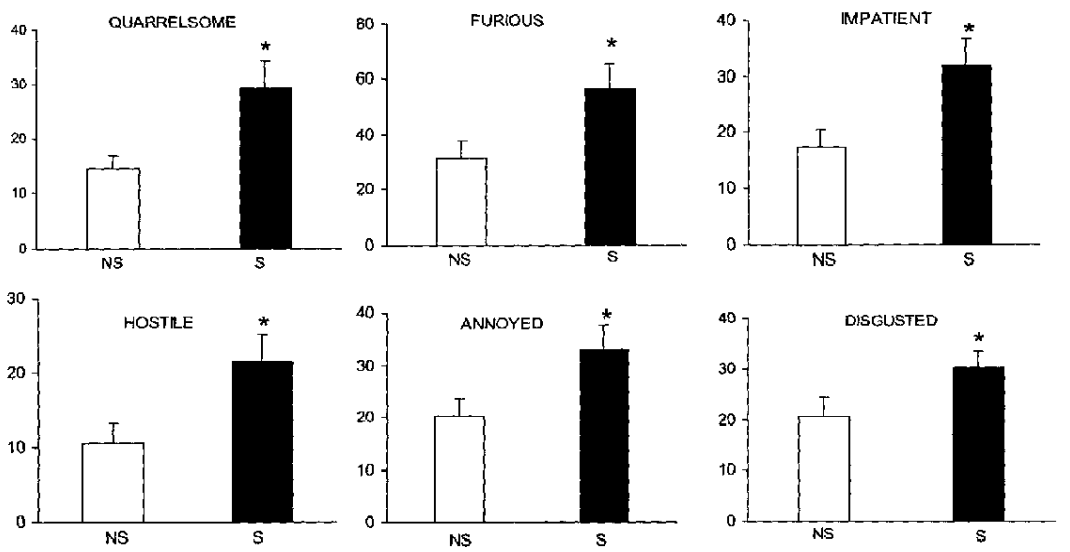

Fig. 2. Mean±S.E.M. analogue ratings (0–100 mm) of feeling quarrelsome, furious, impatient, hostile, annoyed and disgusted by nonsmokers (NS) and smokers (S). * $P<.05$ compared with nonsmokers.

PM3003745714

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

Table 3
Mean ± S.E.M. scores of female and male students on analogue rating scales of bodily symptoms and the mood factors isolated from the Bond and Lader mood scale before (pre) and after (post) exposure to the stress of cognitive testing

	Females		Males	
	Prestress	Poststress	Prestress	Poststress
Sweating *	17.7 ± 4.0	28.6 ± 5.7	10.0 ± 2.7	33.6 ± 5.8
Palpitations *	12.1 ± 2.5	34.9 ± 6.9	11.3 ± 2.1	18.7 ± 4.8
Physical Tiredness *	45.2 ± 6.7	35.4 ± 5.8	28.2 ± 4.7	33.7 ± 5.3
Factor 1 ** Alertness	40.0 ± 3.0	45.2 ± 2.0	47.2 ± 2.6	38.1 ± 3.2
Factor 2*** Discontented	41.6 ± 1.6	50.5 ± 2.3	42.9 ± 1.9	55.8 ± 3.0
Factor 3*** Anxiety	47.1 ± 2.6	71.9 ± 3.4	47.9 ± 3.3	65.2 ± 2.7

* $P < .05$, Sex × Stress interaction.
** $P < .01$, Sex × Stress interaction.
*** $P < .001$, effect of stress.

Smoking Status interaction, $F(1,32) = 5.4$, $P < .03$]. After stress, the smokers, but not the nonsmokers, showed significant increases in ratings of feeling spiteful [Stress × Smoking Status interaction, $F(1,32) = 4.8$, $P < .04$] and rebellious [$F(1,32) = 5.4$, $P < .03$]. After stress, the smokers also showed a greater increase than nonsmokers in their rating of sweating [$F(1,32) = 5.1$, $P < .03$].

3.2.3. Sex differences in response to stress

After stress, several sex differences were found in the students' ratings of bodily symptoms, and all were independent of smoking status (see Table 3). After stress, both sexes showed an increased rating of sweating, but the increase was greater in males [Sex × Stress, $F(1,32) = 4.5$, $P < .05$]. In contrast, the females showed a greater increase in ratings of palpitations [Sex × Stress, $F(1,32) = 6.5$, $P < .02$]. After stress, the females felt less physically tired, whereas the males felt more tired [Sex × Stress, $F(1,32) = 4.8$, $P < .04$].

This same pattern was found on the alertness factor from the Bond and Lader mood scale. After stress, the females felt significantly more alert, whereas the males felt less alert [Sex × Stress, $F(1,32) = 11.3$, $P < .0002$] (see Table 3).

Several individual mood ratings showed sex differences after stress, see Fig. 4. Females felt more alert, clear-headed, energetic, quick-witted, interested, proficient and attentive, whereas males showed changes in the opposite direction [Sex × Stress, $F(1,32) = 9.2$, $P < .005$; 14.1, $P < 001$; 5.8, $P < .02$; 8.6, $P < .01$; 17.7, $P < .0002$; 5.4, $P < .03$; 2.8, $P = .10$, respectively]. Both males and females became less calm after stress, but the change was greater in females [Sex × Stress, $F(1,32) = 5.2$, $P < .03$].

3.3. Cognitive performance

There were no significant effects in performance on the DSS test or on detecting gaps in music (data not shown), but on the other tests, some differences were found that were dependent on both smoking status and sex (see Table 4). For the number of pictures correctly recalled, there was

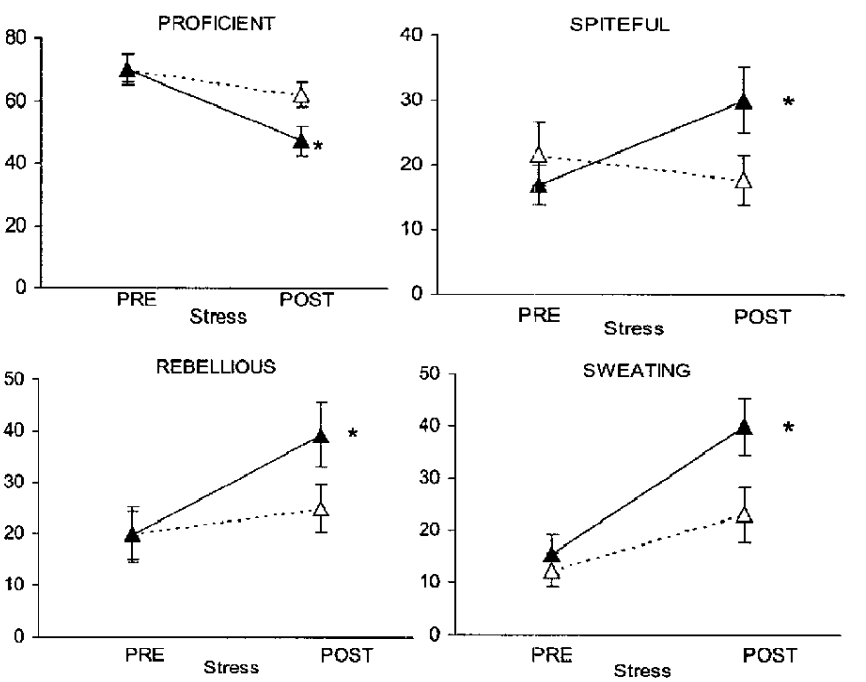

Fig. 3. Mean ± S.E.M. analogue ratings (0–100 mm) of feeling proficient, spiteful, rebellious and sweating before (PRE) and after (POST) the stress of cognitive testing by nonsmokers (△- - - -△) and smokers (▲——▲). * $P < .05$, Smoking × Stress interaction.

PM3003745715
Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

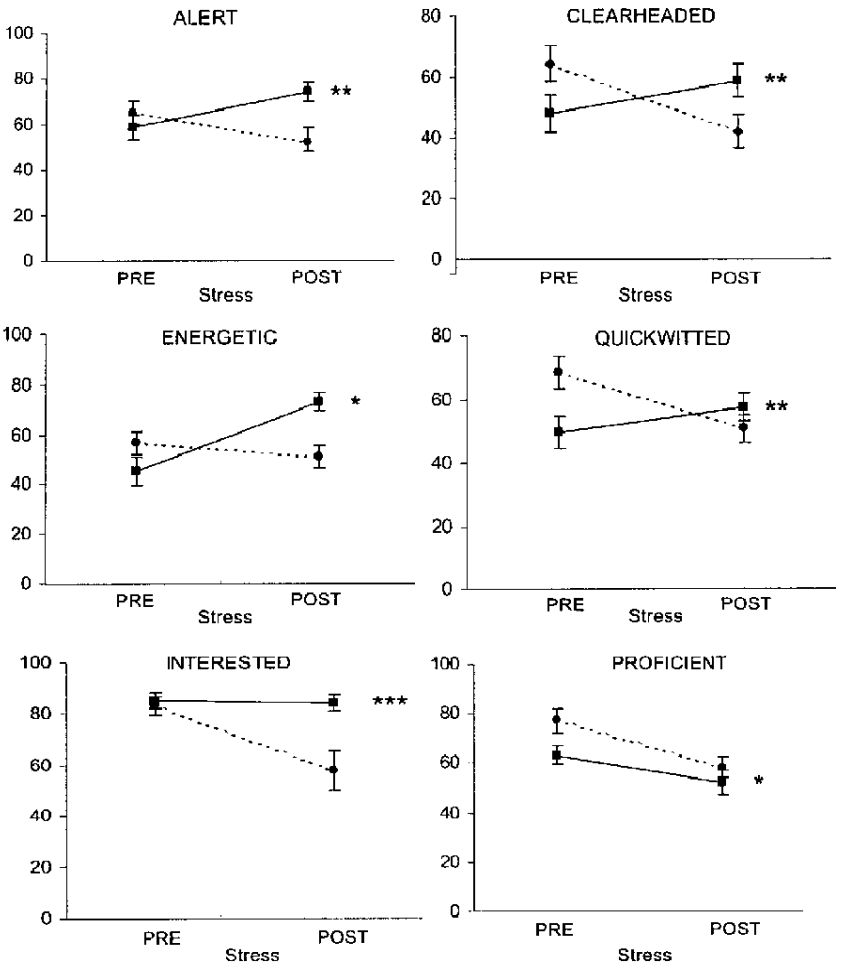

Fig. 4. Mean ± S.E.M. analogue ratings (0–100 mm) of alert, clear-headed, energetic, quick-witted, interested and proficient made before (PRE) and after (POST) the stress of cognitive testing by females ■——■ and males ●- - - - -●. ***$P<.001$, **$P<.01$, *$P<.05$, Sex × Stress interaction.

a significant Smoking × Sex interaction [$F(1,32)=7.0$, $P<.01$], because the female smokers performed better than nonsmokers, whereas the male smokers performed worse than nonsmokers. Thus, the best performance was by female smokers, whereas the male smokers accounted for the worst.

In the DMTS test, there was again a significant Smoking × Sex interaction in the latency to make a correct choice [$F(1,32)=4.1$, $P<.05$]. However, on this occasion, it was the male smokers who performed fastest and the male nonsmokers who were slowest. Similar, but nonsignificant, trends were found for the 4- and 12-s delays [Smoking × Sex, $F(1.32)=2.6$ and 2.0, respectively, ns]. There was a significant sex difference in the number of errors made on the DMTS test, with the females making significantly more errors on shape than males ($z=2.3$, $P<.02$).

In the RVIP test, there was no effect of smoking status on the latency to respond [Smoking, $F(1,32)=1.3$, ns], but the females were significantly slower than males [Sex, $F(1,32)=11.2$, $P<.002$], and this difference was significant on all four blocks of trials in this test. On Block 1, there was a significant Smoking × Sex interaction [$F(1,32)=4.2$, $P<.05$], because the female smokers made significantly fewer hits than the male smokers, but this sex difference was not seen in nonsmokers. A similar pattern was seen in the number of misses on Block 1, with the female smokers significantly worse than the male smokers ($P=.01$), but there was no sex difference in the nonsmokers. With regard to the false alarms, the male smokers made significantly more false alarms than female smokers on Block 1 ($P<.05$) and on false alarms on all four of the blocks ($P<.05$), but there was no sex difference in the nonsmokers.

In the PASAT, there was a significant Speed × Smoking interaction [$F(3,29)=3.0$, $P<.05$], because although the smokers always performed worse than nonsmokers the difference became most marked at the third fastest speed

PM3003745716

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

Table 4
Mean±S.E.M. number of pictures correctly recalled, latency (ms) to make a correct response in the simultaneous condition of the DMTS test, number of shape errors in DMTS, latency (ms) for correct hits in the RVIP test and number of hits, misses and false alarms on Block 1 and correct responses in the PASAT made by female and males smokers and nonsmokers

	Smoker		Nonsmoker	
	Female	Male	Female	Male
Picture Recall***	12.7±0.9	8.8±1.0	9.8±0.9	11.4±1.2
DMTS latency***	2104.9±189.0	1893.1±217.8	1970.3±112.7	2513.3±206.4
Shape Errors****	1.3±0.4	0.4±0.2	1.9±0.7	0.6±0.3
RVIP latency****	1774.7±39.5	1451.3±96.8	1858.9±137.9	1574.7±61.8
Hits Block 1	5.6±0.5*	7.1±0.4	7.3±0.3	7.1±0.5
Misses Block 1	3.4±0.5**	1.9±0.4	1.7±0.3	1.9±0.5
False Alarms	0.2±1.0*	1.0±0.3	0.6±0.2	0.5±0.2
PASAT*****	28.5±1.6	32.3±2.0	33.8±3.6	36.4±2.4

* $P<.05$, compared with male smokers.
** $P<.01$, compared with male smokers.
*** $P<.05$, Smoking × Sex interaction.
**** $P<.05$, sex difference.
***** $P<.05$ smokers versus nonsmokers.

($P<.05$). The worst performance was by female smokers and the best by male nonsmokers (see Table 4).

4. Discussion

Gilbert and Gilbert (1995) reported that smokers had higher levels of neurotic traits (anxiety, depression and anger) than nonsmokers. Our results show that similar differences exist in ratings of current mood state, even when the ratings are made by nondeprived light smokers under baseline conditions. The present results suggest that the mood differences are not restricted to anxiety and depression, but also extend to clear differences in aggressive mood. The mood differences between smokers and nonsmokers were found equally in females and males, and Kassell and Shiffman (1997) also found no sex differences in the effects of smoking on mood. A possibility that should be considered is whether the differences that we have found between our smokers and nonsmokers could have occurred by the chance selection of two groups of 18 medical students. Because of the uniformity in age, IQ and education in our medical students we have shown that the use of an independent group design is as sensitive as a repeated measure design in assessing the effects of benzodiazepines on cognitive performance (File, 1992). The use of an independent group design has also proved sensitive to the cognitive-enhancing effects of glycine (File et al., 1999). In our previous study on nonsmokers in which we used a similar battery of cognitive tests, we found similar levels of anxiety and aggression ratings to those found in the nonsmokers in the present study. It would therefore seem unlikely that a randomly occurring group difference could be the sole explanation of our results.

One of the problems that we encountered was in finding students who smoked cigarettes, but who did not also regularly smoke cannabis. Consumption of recreational drugs was an exclusion factor in our study, but in a future study it would be interesting to compare mood states between smokers of nicotine alone and smokers who smoked both nicotine and cannabis. The design of the present experiment did not allow us to determine whether the differences in mood state between light smokers and nonsmokers were due to constitutional differences between smokers and nonsmokers or whether they were due to long-term effects of nicotine. There is evidence from other studies that both of these factors might be operating (Gilbert and Gilbert, 1995; Sonntag et al., 2000; Perkins et al., 1994; Breslau et al., 1998; West and Hajek, 1997). It was not the purpose of the present study to assess the change in mood in smokers between a deprived and nondeprived state. However, most studies have found that the mood of smokers is worse in the abstinent state than it is after smoking a cigarette or receiving nicotine (Hughes et al., 1984; Parrott, 1994, 1995; Heishman et al., 1994; Warburton and Mancuso, 1998).

Smoking has not always been found to have an anxiolytic effect, and Kassel and Shiffman (1997) found that smoking reduced anxiety only when smokers were engaged in a distracting task. They interpreted this as evidence that the anxiolytic effects of smoking were secondary to improved attention. Thus, smoking enhanced and focussed attention to the cues associated with the task and away from distressing thoughts. Our battery of cognitive tests would have certainly occupied the volunteers' attention, but there was no evidence of the smokers experiencing reduced anxiety compared with nonsmokers. In fact, they experienced even greater negative mood changes. Could an explanation of this be that the smokers had enhanced attention to the tests, which were themselves a source of anxiety? The results from the cognitive tests provided no evidence that the smokers had enhanced attention compared with the nonsmokers. There was no difference in performance of the test of divided attention and smokers did not perform better in either of the

PM3003745717

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

tests of sustained attention. However, it remains possible that the smokers attended more to the distressing aspects of the test than did the nonsmokers.

We found that our light nondeprived smokers performed no better than nonsmokers in the memory tests, which agrees with the previous findings of Phillips and Fox (1998). We also found no evidence of better performance by smokers in tests of attention and they performed worse in PASAT. This is similar to the finding of Spilich et al. (1992) that nondeprived smokers performed worse than nonsmokers in a test of sustained attention. These results are not in conflict with studies that have shown that nicotine improves performance in both smokers and nonsmokers (Wesnes and Warburton, 1978, 1984; Wesnes et al., 1983; Provost and Woodward, 1991; Foulds et al., 1996; Mancuso et al., 1999), since these used abstinent smokers. For example, nicotine improved performance in the RVIP test in abstinent smokers (Mancuso et al., 1999; Foulds et al., 1996; Warburton and Mancuso, 1998).

The main purpose of the present experiment was to explore possible sex differences in the mood of smokers and nonsmokers, and especially the way in which these might be revealed after the stress of cognitive testing. We had previously found (File et al., 2000, 2001) that nicotine administration to nonsmokers had calming effects in women, but enhanced anxiety and aggressive feelings in males. This pattern of results was not found when we compared smokers and nonsmokers. In both sexes, smokers were found to feel more discontented, troubled and aggressive, and these differences were further enhanced by the stress of cognitive testing. In a similar study, when mood ratings were made after cognitive tests, Netter et al. (1998) found that smoking increased feelings of arousal and emotional tension in nondeprived female smokers. In those with higher neuroticism scores, smoking also increased ratings of anxiety and sadness. Whilst there may well be beneficial mood effects that result from smoking reversing the adverse effects of withdrawal (e.g. Hughes et al., 1984), and in conditions in which smokers are engaged in a benign distracting task (Kassel and Shiffman, 1997), the results of the present study suggest that these are by no means universal. Indeed, the enhanced aggressive mood that was evident even at baseline in our group of light, nonabstinent smokers suggests that it might be a quite prevalent finding.

The most recent studies on individual propensity to smoking have found that smoking is influenced by an interaction between neuroticism and the 5-HTTLPR-S genotype of the 5-HT transporter gene (Lerman et al., 2000; Hu et al., 2000). This is particularly interesting, since animal studies have shown that both nicotine's anxiolytic and anxiogenic effects are mediated by the 5-HT system (Kenny et al., 2000; Cheeta et al., 2000, 2001). We do not yet know whether nicotinic modulation of aggression is mediated by the 5-HT system, but there is considerable evidence for an interaction between anxiety, the 5-HT system and aggressive behaviour (Rodgers, 1991). Thus, the mood differences that we have found between smokers and nonsmokers may be the result of both genetic factors and direct effects of nicotine, mediated by the 5-HT system.

References

Anda RF, Croft JB, Felitti VJ, Nordenberg D, Giles WH, Williamson DF, Giovino GA. Adverse childhood experiences and smoking during adolescence and adulthood. JAMA, J Am Med Assoc 2000;283: 1958–9.

Bond AJ, Lader MH. The use of analogues scales in rating subjective feelings. Br J Med Psychol 1974;47:211–21.

Bond AJ, Lader M. A method to elicit aggressive feelings and behaviour via provocation. Biol Psychol 1986;22:69–79.

Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski P. Major depression and stages of smoking: a longitudinal investigation. Arch Gen Psychiatry 1998;55:161–6.

Cheeta S, Kenny PJ, File SE. The role of 5-HT_{1A} receptors in mediating the anxiogenic effects of nicotine following lateral septal administration. Eur J Neurosci 2000;12:3797–802.

Cheeta S, Irvine EE, Kenny PJ, File SE. The dorsal raphe nucleus is a crucial structure mediating nicotine's anxiolytic effects and the development of tolerance and withdrawal responses. Psychopharmacology 2001;155:78–85.

Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Questionnaire. San Diego, London: Hodder and Stoughton, 1976.

File SE. Effects of lorazepam on psychomotor performance: a comparison of independent groups and repeated measures designs. Pharmacol, Biochem Behav 1992;42:761–4.

File SE, Kenny PJ, Ouagazzal A-M. Bimodal modulation by nicotine of anxiety in the social interaction test: role of dorsal hippocampus. Behav Neurosci 1998;112:1423–9.

File SE, Fluck E, Fernandes C. Beneficial effects of glycine (Bioglycin) on memory and attention in young and middle-aged adults. J Clin Psychopharmacol 1999;19:506–12.

File SE, Fluck E, Leahy A. Nicotine and stress induced mood changes in female and male non smokers. Br J Pharmacol 2000;50:384.

File SE, Fluck E, Leahy A. Nicotine has calming effects on stress induced mood changes in females, but enhances aggressive mood in males. Int J Neuropsychopharmacol 2001;4:371–6.

Foulds J, Stapleton J, Swettenham J, Bell N, McSorley K, Russell MA. Cognitive performance effects of subcutaneous nicotine in smokers and never-smokers. Psychopharmacology 1996;127:31–8.

Gilbert DG, Gilbert BO. Personality, psychopathology, and nicotine response as mediators of the genetics of smoking. Behav Genet 1995; 25:133–47.

Heishman SJ, Taylor RC, Henningfield JE. Nicotine and smoking: a review of effects on human performance. Exp Clin Psychopharmacol 1994;2: 345–95.

Hu S, Brody CL, Fisher C, Gunzerath L, Nelson ML, Sabol SZ, Sirota LA, Marcus SE, Greenberg BD, Murphy DL, Hamer DH. Interaction between the serotonin transporter gene and neuroticism in cigarette smoking behavior. Mol Psychiatry 2000;5:181–8.

Hughes JR, Hatsukami DK, Pickens RW, Krahn D, Malin S, Luknic A. Effect of nicotine on the tobacco withdrawal syndrome. Psychopharmacology 1984;83:82–7.

Hughes JR, Gust SW, Keenan RM, Fenwick JW. Effect of dose on nicotine's reinforcing, withdrawal-suppression and self-reported effects. J Pharmacol Exp Ther 1990;252:1175–83.

Hughes JR, Gust SW, Skoog K, Keenan RM, Fenwick JW. Symptoms of tobacco withdrawal. A replication and extension. Arch Gen Psychiatry 1991;48:52–9.

Kassel JD, Unrod M. Smoking, anxiety and attention: Support for the role of nicotine in attentionally mediated anxiolysis. J Abnormal Psychol 2000;109:161–6.

PM3003745718

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001

Kenny PJ, Cheeta S, File SE. Anxiogenic effects of nicotine in the dorsal hippocampus are mediated by 5-HT_{1A} and not by muscarinic M_1 receptors. Neuropharmacology 2000;39:300–7.

Lerman C, Caporaso NE, Audrain J, Main D, Boyd NR, Shields PG. Interacting effects of the serotonin transporter gene and neuroticism in smoking practices and nicotine dependence. Mol Psychiatry 2000; 5:189–92.

Mancuso G, Andres P, Ansseau M, Tirelli E. Effects of nicotine administered via a transdermal delivery system on vigilance: a repeated measure study. Psychopharmacology 1999;142:18–23.

Martin CA, Logan TK, Portis C, Leukefeld CG, Lynam D, Brogli B, Flory K, Clayton RR. The association of testosterone with nicotine use in young adult females. Addict Behav 2001;26:279–83.

Nelson HE, Willison JR. Restandardisation of the NART against the WAIS-R. Windsor: NFER-Nelson, 1991.

Netter P, Hennig J, Huwe S, Olbrich R. Personality related effects of nicotine, mode of application, and expectancies on performance, emotional states, and desire for smoking. Psychopharmacology 1998;135: 52–62.

Owen AM, Sahakian BJ, Semple J, Polkey CE, Robbins TW. Visuo-spatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. Neuropsychologia 1995;33:1–24.

Parrott AC. Acute pharmacodynamic tolerance to the subjective effects of cigarette smoking. Psychopharmacology 1994;116:93–7.

Parrott AC. Stress modulation over the day in cigarette smokers. Addiction 1995;90:233–44.

Parrott AC. Does cigarette smoking cause stress? Am Psychol 1999;54: 817–20.

Perkins KA, Sexton JE, Stiller RL, Fonte C, DiMarco A, Goettler J, Sclerka A. Subjective and cardiovascular responses to nicotine combined with caffeine during rest and casual activity. Psychopharmacology 1994;113: 438–44.

Perkins KA, Donny E, Caggiula AR. Sex differences in nicotine effects and self-administration: review of human and animal evidence. Nicotine Tob Res 1999;1:301–15.

Phillips S, Fox P. An investigation into the effects of nicotine gum on short-term memory. Psychopharmacology 1998;140:429–33.

Provost SC, Woodward R. Effects of nicotine gum on repeated administration of the Stroop test. Psychopharmacology 1991;104:536–40.

Quattrocki E, Baird A, Yurgelin-Todd D. Biological aspects of the link between smoking and depression. Harv Rev Psychiatry 2000;8:99–110.

Rodgers RJ. Effects of benzodiazepine and 5-HT receptor ligands on aggression and defence in animals. In: Rodgers RJ, Cooper SJ, editors. 5-HT1A agonists, 5-HT3 antagonists and benzodiazepines. Their comparative behavioural pharmacology. Chichester, UK: Wiley, 1991. pp. 195–231.

Royal College of Physicians. Nicotine addiction in Britain: a report of the tobacco advisory group. Suffolk: Lavenham Press, 2000.

Sonntag E, Wittchen HU, Hofler M, Kessler RC, Stein MB. Are social fears and DSM-IV social anxiety disorder associated with smoking and nicotine dependence in adolescents and young adults? Eur Psychiatry 2000;1:67–74.

Spielberger CD, Jacobs BA. Pesonality and smoking behavior. J Pers Assess 1982;46:396–403.

Spilich GJ, June L, Renner J. Cigarette smoking and cognitive performance. Br J Addict 1992;87:1313–26.

Spreen O, Strauss E. A compendium of neuropsychological tests: administration norms and Commentary. Oxford: Oxford Univ. Press, 1991.

Warburton DM, Mancuso G. Evaluation of the information processing and mood effects of a transdermal nicotine patch. Psychopharmacology 1998;135:305–10.

Weschler D. Wechsler Adult Intelligence Scale-Revised. Chicago: Psychological Corporation, Harcourt Brace Jovanovich, 1981.

Wesnes K, Warburton DM. The effects of cigarette smoking and nicotine tablets upon human attention. In: Thornton RE, editor. Smoking behavior: physiological and psychological influences. London: Churchill-Livingstone, 1978. pp. 131–47.

Wesnes K, Warburton DM. Effects of smoking on rapid information processing performance. Neuropsychobiology 1983;9:223–9.

Wesnes K, Warburton DM. The effects of cigarettes of varying yield on rapid information processing performance. Psychopharmacology 1984; 82:338–42.

Wesnes K, Warburton DM, Matz B. Effects of nicotine on stimulus sensitivity and response bias in a visual vigilance task. Neuropsychobiology 1983;9:41–4.

West RJ, Hajek P. What happens to anxiety levels on giving up smoking? Am J Psychiatry 1997;154:1589–92.

Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361–70.

PM3003745719

Source: https://www.industrydocuments.ucsf.edu/docs/nrlj0001